



ACY33316-D3

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicant:** Sridhar Krishna Rabindran et al

**Appl. No.:**

(Divisional of Serial Number 09/321,182)

**Filed:** February 28, 2002

**Title:** REVERSAL OF MULTIDRUG RESISTANCE IN HUMAN COLON  
CARCINOMA CELLS

**Grp/A.U.:**

**Examiner:**

**Docket No:** ACY33316-D3

February 28, 2002

Honorable Commissioner of Patents  
Washington, D.C. 20231

**PRELIMINARY AMENDMENT**

Sir:

Preliminary to the examination of the above-identified patent application,  
please amend the application as follows:

**In the Specification:**

Please replace the paragraph beginning at line 18 on page 1 with the following  
rewritten paragraph:

- - This application is a divisional application of copending application Serial  
Number 09/321,182, filed May 27, 1999 which claims benefit of prior U.S.  
Provisional application Number, 60/109,801 which was converted from U.S. Patent  
Application Number 09/085,549 filed May 27, 1998, pursuant to a petition filed under  
37C.F.R. 1.53(C)(2) on November 2, 1998. These applications are herein  
incorporated by reference in their entireties.- -

Please replace the paragraph page 32, lines 12-17 as follows:

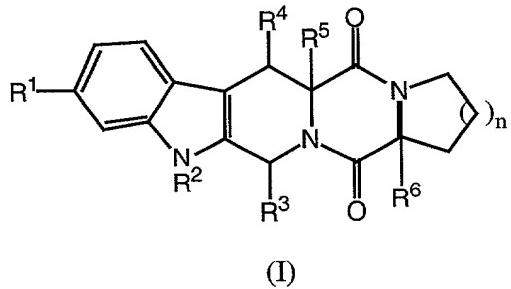
--A viable culture of this new producing strain was deposited with the Culture Collection Laboratory, Northern Utilization Research and Development Division, U.S. Department of Agriculture, Peoria, Ill. on June 7, 1999 and added to its permanent collection under accession number NRRL-30140 in accordance with the Budapest Treaty and is freely available to the public from this depository.--

IN THE CLAIMS

Please cancel Claims 1, 7, 13-28, 34-38, 44-54, 57-59, 61 and 63 without prejudice.

Amend Claim 55 as follows:

55. (Amended) The method according to claim 2 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



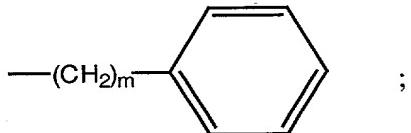
wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms, R<sup>7</sup>NH(CH<sub>2</sub>)<sub>v</sub>- or

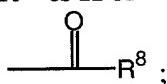


m is an integer of 1 to 6;

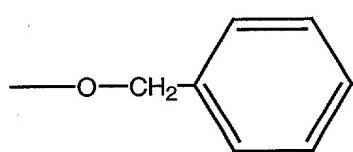
v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

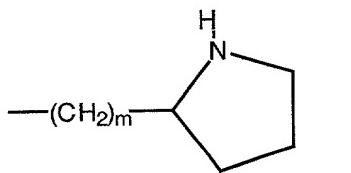
$R^7$  is H or



$R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $-(CH_2)_mCO_2H$ ,



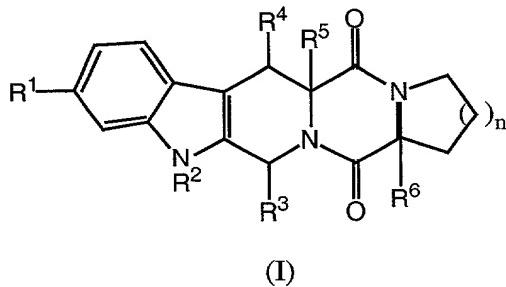
and



or a pharmaceutically acceptable salt thereof.

Amend Claim 56 as follows:

56. (Amended) The method according to claim 8 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



wherein:

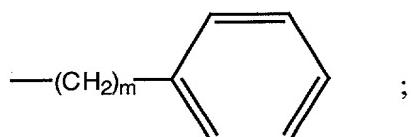
$n$  is an integer of 0, 1, or 2;

$R^1$  is hydrogen or alkoxy of 1 to 10 carbon atoms;

$R^2$  is hydrogen or alkenyl of 2 to 10 carbon atoms;

$R^3$  is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

$R^7NH(CH_2)_v-$  or

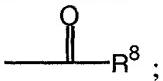


m is an integer of 1 to 6;

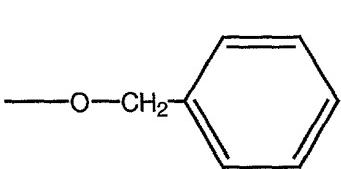
v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

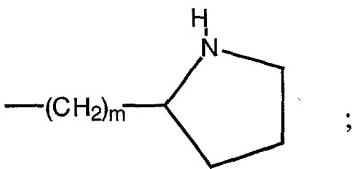
R<sup>7</sup> is H or



R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,



and

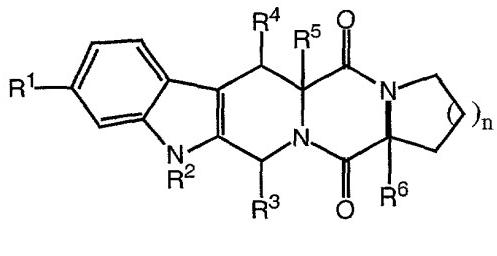


;

or a pharmaceutically acceptable salt thereof.

Amend Claim 60 as follows:

60. (Amended) A method according to claim 29 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



(I)

wherein:

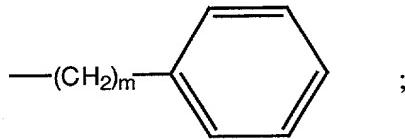
n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH<sub>2</sub>)<sub>v</sub>- or

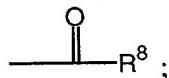


m is an integer of 1 to 6;

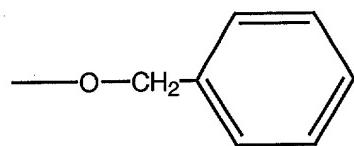
v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

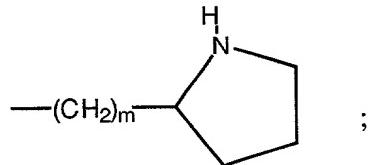
R<sup>7</sup> is H or



R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,



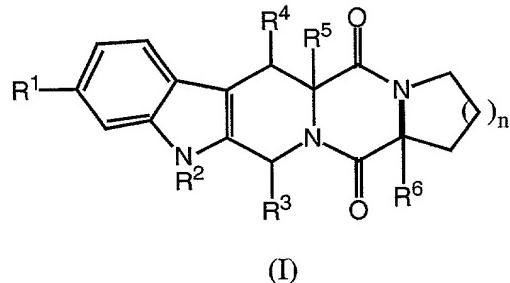
and



or a pharmaceutically acceptable salt thereof.

Amend Claim 62 as follows:

62. (Amended) A method according to claim 39 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I)



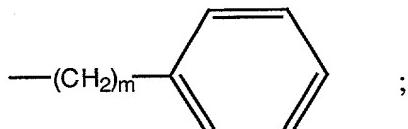
wherein:

n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

$R^3$  is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,  
 $R^7NH(CH_2)_v-$  or

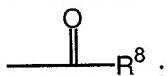


$m$  is an integer of 1 to 6;

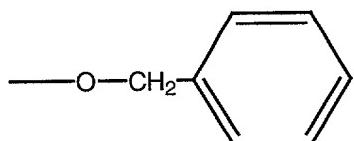
$v$  is an integer of 1 to 4;

$R^4$ ,  $R^5$  and  $R^6$  are hydrogen;

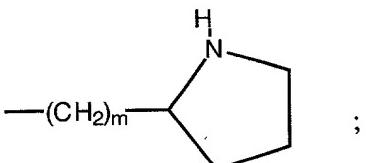
$R^7$  is H or



$R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $-(CH_2)_mCO_2H$ ,



and



or a pharmaceutically acceptable salt thereof.

#### REMARKS

The present application is a divisional application of U.S. Serial No. 09/321,182. The specification has been amended to reflect the complete prosecution history.

#### AMENDMENT PETITION UNDER 37 CFR 1.48(b).

Attached hereto is an amendment petition under 37 CFR 1.48(b) to delete the name of Maya Prakash Singh as a co-inventor of the claims presently being prosecuted so that only the true inventors are named.

The accession number NRRL-30140 assigned by the Culture Collection Laboratory, Northern Utilization Research and Development Division, U.S. Department of

Agriculture, Peoria, Ill. has been added to the specification by amending the specification on page 32, lines 12-17.

Applicants have additionally selected claim 62 to also be prosecuted.

Attached hereto is a marked-up version of changes made to the specification and claims by the current amendment. The attached page is captioned "Version with markings to show changes made."

In view of the foregoing preliminary amendments and remarks, it is respectfully submitted that the present application is in condition for allowance and early notification thereof is earnestly solicited.

Respectfully submitted,



Daniel B. Moran  
Registration No. 41,204  
Agent for the Applicants

American Home Products  
Patent Law Department  
5 Giralda Farms  
Madison, New Jersey 07940  
(845) 602-2224

**VERSION WITH MARKINGS TO SHOW CHANGES MADE  
IN THE SPECIFICATION**

Paragraph beginning on page 1, line 18 has been amended as follows:

This application is a divisional application of copending application Serial Number 09/321,182, filed May 27, 1999 which claims the benefit of prior U.S. Provisional Application №. Number 60/109,801 which was converted from U.S. Patent Application Number №. 09/085,549 filed May 27, 1998, pursuant to a petition filed under 37 C.F.R. 1.53(c)(2) on November 2, 1998. These applications are herein incorporated by reference in their entireties.

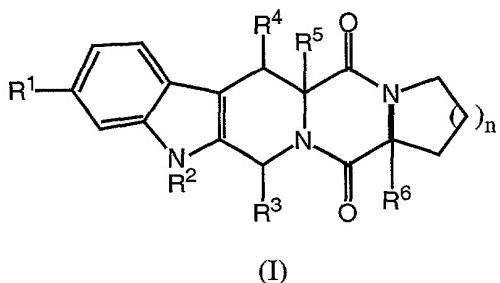
Paragraph beginning on page 32, lines 12-17 has been amended as follows:

A viable culture of this new product producing stain [will be sent for deposit] was deposited with the Culture Collection Laboratory, Northern Utilization Research and Development Division, U.S. Department of Agriculture, Peoria, Ill. on June [4] 7, 1999 and [will be] added to its permanent collection under accession number [{NRRL- }] NRRL-30140 in accordance with the Budapest Treaty and is freely available to the public from this depository.

**IN THE CLAIMS**

Claims 1, 7, 13-28, 34-38, 44-54, 57-59, 61 and 63 have been canceled.

55. (Amended) The method according to claim 2 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



wherein:

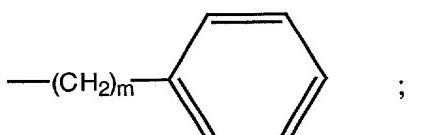
n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH<sub>2</sub>)<sub>v</sub>- or

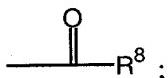


m is an integer of 1 to 6;

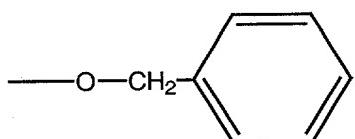
v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

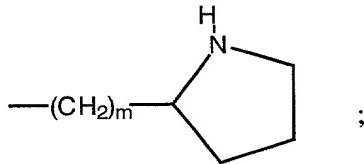
R<sup>7</sup> is H or



R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,



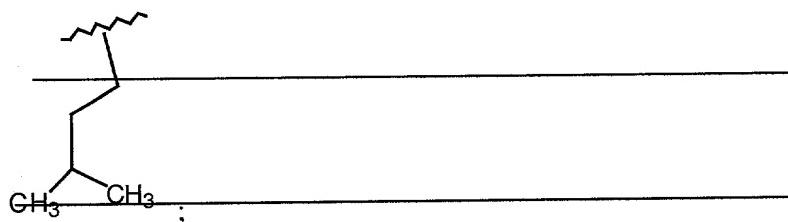
and

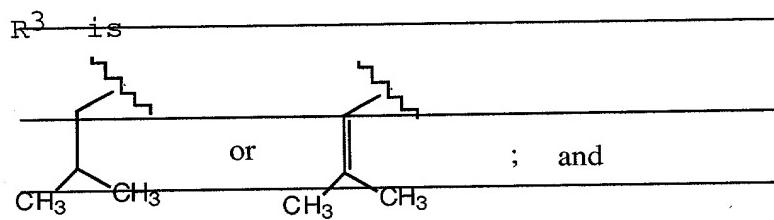


with the proviso that n is not 1 when

a. R<sup>1</sup> is H or CH<sub>3</sub>O;

b. R<sup>2</sup> is H or



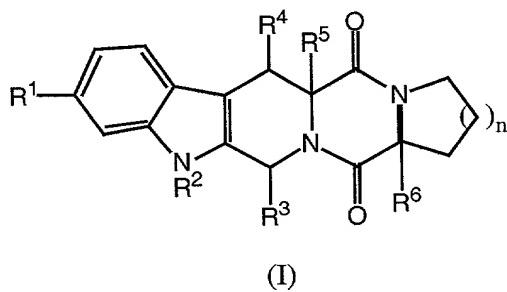


$R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

or a pharmaceutically acceptable salt thereof.

Claim 56 has been amended as follows:

56. (Amended) A method according to claim 8 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



wherein:

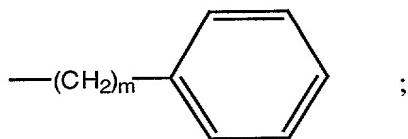
$n$  is an integer of 0, 1, or 2;

$R^1$  is hydrogen or alkoxy of 1 to 10 carbon atoms;

$R^2$  is hydrogen or alkenyl of 2 to 10 carbon atoms;

$R^3$  is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

$R^7NH(CH_2)^v-$  or

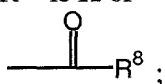


$m$  is an integer of 1 to 6;

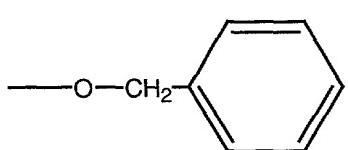
$v$  is an integer of 1 to 4;

$R^4$ ,  $R^5$  and  $R^6$  are hydrogen;

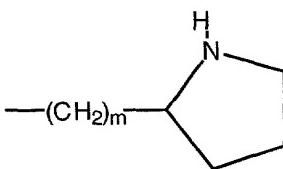
$R^7$  is H or



$R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $-(CH_2)_mCO_2H$ ,



and

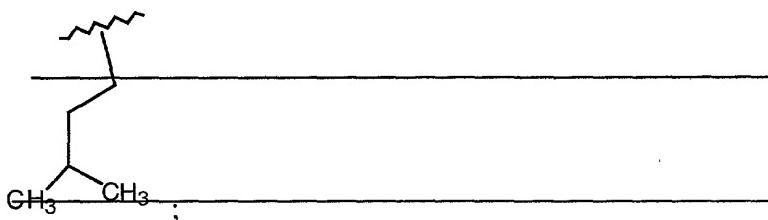


;

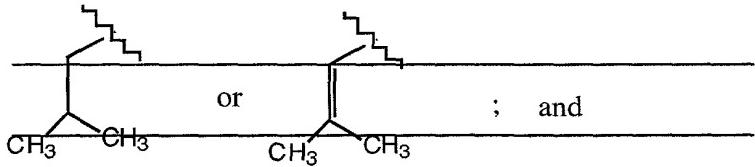
with the proviso that n is not 1 when

a.  $R^1$  is H or  $CH_3O$ ;

$R^2$  is H or



$R^3$  is

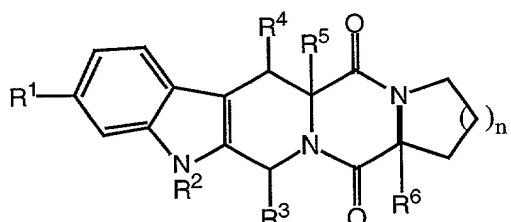


$R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

or a pharmaceutically acceptable salt thereof.

Claim 60 has been amended as follows:

60. (Amended) A method according to claim 29 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



(I)

wherein:

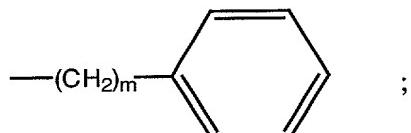
n is an integer of 0, 1, or 2;

R<sup>1</sup> is hydrogen or alkoxy of 1 to 10 carbon atoms;

R<sup>2</sup> is hydrogen or alkenyl of 2 to 10 carbon atoms;

R<sup>3</sup> is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

R<sup>7</sup>NH(CH<sub>2</sub>)<sub>v</sub>- or

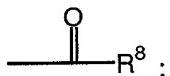


m is an integer of 1 to 6;

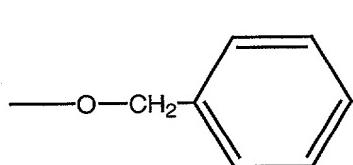
v is an integer of 1 to 4;

R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen;

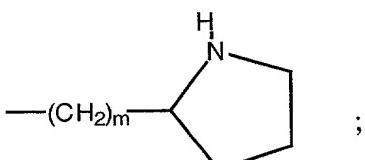
R<sup>7</sup> is H or



R<sup>8</sup> is selected from alkyl of 1 to 10 carbon atoms, -(CH<sub>2</sub>)<sub>m</sub>CO<sub>2</sub>H,



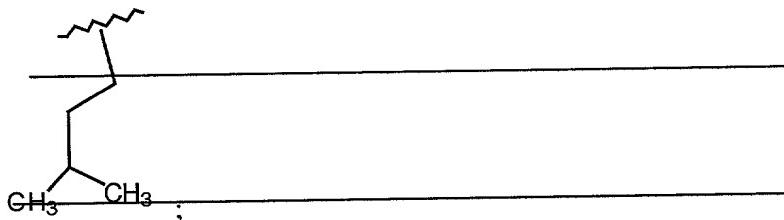
and



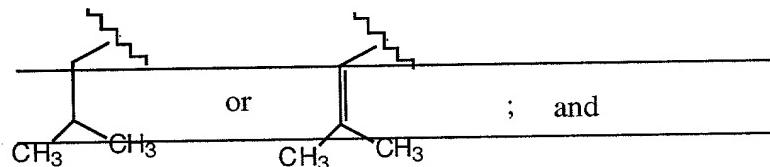
with the proviso that n is not 1 when

a.  $R^1$  is H or  $CH_3O$ ;

$R^2$  is H or



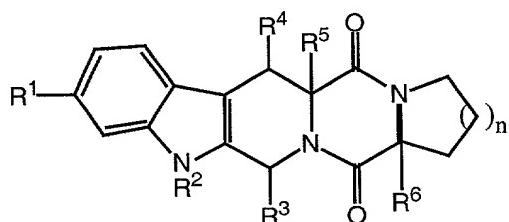
$R^3$  is



$R^4$ ,  $R^5$  and  $R^6$  are hydrogen; and

or a pharmaceutically acceptable salt thereof.

62. (Amended) A method according to claim 39 wherein the chemosensitizing reversal agent is selected from a compound having the Formula (I).



(I)

wherein:

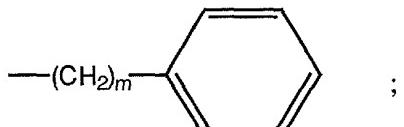
n is an integer of 0, 1, or 2;

$R^1$  is hydrogen or alkoxy of 1 to 10 carbon atoms;

$R^2$  is hydrogen or alkenyl of 2 to 10 carbon atoms;

$R^3$  is hydrogen, alkyl of 1 to 10 carbon atoms, alkenyl of 2 to 10 carbon atoms,

$R^7NH(CH_2)v-$  or

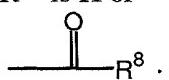


$m$  is an integer of 1 to 6;

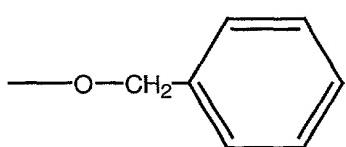
$v$  is an integer of 1 to 4;

$R^4$ ,  $R^5$  and  $R^6$  are hydrogen;

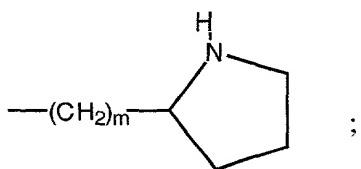
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$R^8$  is selected from alkyl of 1 to 10 carbon atoms,  $-(CH_2)_mCO_2H$ ,



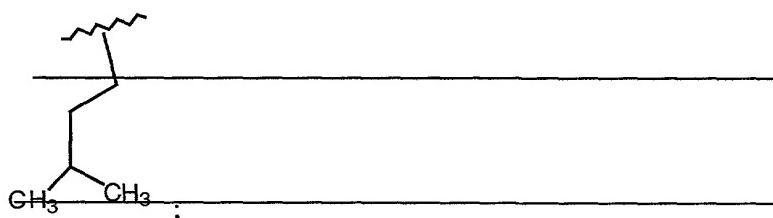
and



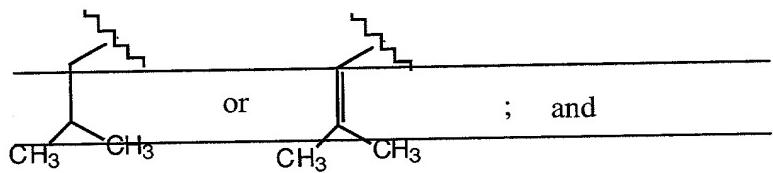
with the proviso that  $n$  is not 1 when

a.  $R^1$  is H or  $CH_2O$ ;

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R<sup>4</sup>, R<sup>5</sup> and R<sup>6</sup> are hydrogen; and

or a pharmaceutically acceptable salt thereof.

2002  
0409 US PTO



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ACY33316-D3

**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE**

**Applicant:** Sridhar Krishna Rabindran et al  
**Appl. No.:**  
**(Divisional of Serial Number 09/321,182)**  
**Filed:** February 28, 2002  
**Title:** REVERSAL OF MULTIDRUG RESISTANCE IN HUMAN COLON CARCINOMA CELLS

**Grp/A.U.:**

**Examiner:**

**Docket No:** ACY33316-D3

February 28, 2002

Honorable Commissioner of Patents  
Washington, D.C. 20231

**AMENDMENT PETITION AND FEE DELETING CORRECTLY NAMED ORIGINAL PERSON WHO IS NOT AN INVENTOR OF INVENTION NOW BEING CLAIMED (37 CFR 1.48(b))**

Sir:

1. This amendment and petition under 37 CFR 1.48(b), is to delete the name of

\*\*\*\*\*

CERTIFICATE OF MAILING BY "EXPRESS MAIL"  
"EXPRESS MAIL" MAILING LABEL NUMBER ET372497923US

DATE OF DEPOSIT \_\_\_\_\_

I HEREBY CERTIFY THAT THIS PAPER OR FEE IS BEING DEPOSITED WITH THE UNITED STATES POSTAL SERVICE BY "EXPRESS MAIL" POST OFFICE TO ADDRESSEE SERVICE UNDER 37 C.F.R. 1.10 ON THE DATE INDICATED ABOVE AND IS ADDRESSED TO THE COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231

DATE: February 28, 2002

Daniel B. Morris

(TYPED OR PRINTED NAME OF PERSON MAILING PAPER OR FEE)

Daniel B. Morris

(SIGNATURE OF PERSON MAILING PAPER OR FEE)

the following person named as inventor and who is not the inventor of the invention now being claimed:

Maya Prakash Singh

## 2. Claims now on File

The claims in this divisional application are as follows:

Originally filed claims 1-63 in Serial Number 09/321,182 were restricted as per the Office Letter of September 28, 2000 into VI Groups.

Claims 2-6, 8-12, 29-33, 39-43, 60, and 62 of restriction Group IV are elected for prosecution in the present divisional as well as Claims 55 and 56.

## 3. Status of Inventorship After Amendment

This amendment and petition is being filed in order to ensure that the correct co-inventors will be named in the above-identified application, in which Claims 1-63 of Serial Number 09/321,182 are pending. Maya Prakash Singh is a co-inventor of the subject matter of originally filed Claims 1-63, however, the above named inventor Maya Prakash Singh is not a co-inventor of the subject matter now embraced by this divisional application. However, since Claims 2-6, 8-12, 29-33, 39-43, 60, and 62 as well as 55 and 56 will be under consideration in the present divisional application, it is imperative to delete Maya Prakash Singh from the instant application, so that only the true inventors are named. It is respectfully requested that Maya Prakash Singh be deleted from the instant application.

## 4. Fee

Please charge Deposit Account No. 01-1300 the sum of \$130.00 to pay the fee required by 37 CFR 1.17(h).

Respectfully submitted,



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